

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Claims 1-21 (cancelled)

Claim 22 (currently amended): A composition comprising a plurality of a conjugate, wherein said conjugate is formable by the conjugation of:

(a) a $\text{-OCH}_2\text{CH}_2\text{O-}$ $\text{-CH}_2\text{OCH}_2\text{-}$ containing chemically defined valency platform molecule comprising a moiety selected from $\text{-CH}_2(\text{CH}_2\text{OCH}_2)_r\text{CH}_2\text{-}$, 2,2'-ethylenedioxydiethylamine, triethylene glycol, and polyethylene glycol having a molecular weight of about 200 to about 8,000, wherein:

~~$r = 0$ to 300;~~

$r = 1$ to 300;

the moiety is derivatized with branching groups;

the valency of said platform molecule is provided by at least four but no more than 32 ~~or more~~ attachment sites located at termini of the valency platform molecule;

~~the valency platform molecule has a single line of symmetry; and~~

the valency platform molecule is chemically defined in that the number of branching groups pre-determines the number of attachment sites for biologically active molecules; ~~and~~

(b) a multiplicity of biologically active molecules; and;

(c) linker groups that bind the valency platform molecule to the biologically active molecules, wherein the multiplicity of biologically active molecules is conjugated to the chemically defined valency platform molecule via the linker groups at said attachment sites.

Claim 23 (previously presented): The composition of claim 22, wherein the branching groups are derived from a functional moiety selected from the group consisting of diamino acid, triamine, and amino diacid.

Claim 24 (cancelled)

Claim 25 (cancelled)

Claim 26 (previously presented): The composition of claim 22, wherein the biologically active molecules comprise a polynucleotide.

Claim 27-31 (cancelled)

Claim 32 (currently amended): The composition of claim 22, wherein the biologically active molecules are selected from the group consisting of carbohydrates, lipids, lipopolysaccharides, peptides, proteins, glycoproteins, single-stranded oligonucleotides, double-stranded oligonucleotides, analogs of an immunogen, haptens, mimotopes, aptamers, polynucleotides and drugs.

Claim 33-34 (cancelled)

Claim 35 (previously presented): The composition of claim 22, wherein the composition comprises a pharmaceutically acceptable carrier.

Claim 36 (currently amended): The composition of claim 35, wherein the composition is suitable for the suppression of antibody production in an individual.

Claim 37 (cancelled)

Claim 38 (cancelled)

Claim 39-42 (cancelled)

Claim 43 (previously presented): The composition of claim 22, wherein the valency platform molecule comprises triethylene glycol.

Claim 44 (cancelled)

Claim 45 (previously presented): A method of making the composition of claim 22, wherein the biologically active molecules are a polynucleotide duplex, the method comprising forming said conjugates by:

reacting a multiplicity of single-stranded polynucleotides, each of which is at least 20 nucleotides in length and has a functional group at or proximate one of its termini, with functional groups on the chemically-defined valency platform molecule to form the conjugate; and annealing complementary single-stranded polynucleotides to the single-stranded polynucleotides conjugated to the chemically-defined valency platform molecule to form pendant chains of double-stranded polynucleotides.

Claim 46 (previously presented): The composition of claim 22, wherein the conjugate comprises triethyleneglycol.

Claim 47-50 (cancelled)

Claim 51 (currently amended): The composition of claim 35, wherein the composition is suitable for reducing antibody levels in an individual.

Claim 52 (previously presented): The composition of claim 35 wherein at least one molecule of the biologically active molecules is an analog of an immunogen that binds specifically to an antibody to which the immunogen binds specifically and lacks T cell epitopes.

Claim 53 (currently amended): The composition of claim 22 or 52 ~~22 or 64~~, wherein the composition is suitable for reducing antibody levels in an individual.

Claim 54 (currently amended): The composition of claim 22, wherein the conjugate comprises linking groups derived from an alkylsulfhydryl moiety and the attachment sites comprise thiophilic groups ~~moieties bound to the valency platform molecule and to the biologically active molecules~~.

Claims 55-63 (cancelled)

Claim 64 (currently amended): A composition comprising a plurality of a conjugate, wherein said conjugate is formable by the conjugation of:

(a) a $\text{-OCH}_2\text{CH}_2\text{O-}$ $\text{-CH}_2\text{OCH}_2\text{-}$ containing chemically defined valency platform molecule comprising a moiety selected from $\text{-CH}_2(\text{CH}_2\text{OCH}_2)_r\text{CH}_2\text{-}$, 2,2'-ethylenedioxydiethylamine, triethylene glycol, and polyethylene glycol having a molecular weight of about 200 to about 8,000, wherein:

~~$r = 0$ to 300;~~

$r = 1$ to 300;

the moiety is derivatized with branching groups provided that when the $\text{-CH}_2\text{OCH}_2\text{-}$ containing chemically defined valency platform molecule comprises a moiety selected from $\text{-CH}_2(\text{CH}_2\text{OCH}_2)_r\text{CH}_2\text{-}$ or polyethylene glycol having a molecular weight of about 200 to about 8,000, the branching group is selected from the group consisting of diamino acid, triamine, and amino diacid groups;

the valency of said platform molecule is provided by at least four but no more than 32~~or more~~ attachment sites located at termini of the valency platform molecule; and

the valency platform molecule is chemically defined in that the number of branching groups pre-determines the number of attachment sites for biologically active molecules; and

(b) a multiplicity of biologically active molecules conjugated to the chemically defined valency platform molecule at said attachment sites.

Claim 65 (previously presented): The composition of claim 64, wherein the valency platform molecule has a single line of symmetry.

Claim 66 (previously presented): The composition of claim 64, wherein the biologically active molecules are the same.

Claim 67 (previously presented): The composition of claim 64 or 66, wherein said conjugate comprises two branching groups, providing a total of four attachment sites for the biologically active molecules.

Claim 68 (previously presented): The composition of claim 64, wherein the biologically active molecules comprise a polynucleotide.

Claim 69 (previously presented): The composition of claim 68, wherein the polynucleotide is a polynucleotide duplex.

Claim 70 (previously presented): The composition of claim 68, wherein the polynucleotide is a polynucleotide duplex of about 20 to about 50 base pairs in length.

Claim 71 (previously presented): The composition of claim 68, wherein the polynucleotide is synthetic.

Claim 72 (previously presented): The composition of claim 68, wherein the polynucleotide is prepared by molecular cloning.

Claim 73 (previously presented): The composition of claim 68, wherein the polynucleotide is a polynucleotide duplex having a B DNA type helical structure.

Claim 74 (previously presented): The composition of claim 64, wherein the branching groups are derived from a functional moiety selected from the group consisting of diamino acid, triamine, and amino diacid.

Claim 75 (currently amended): The composition of claim 64, wherein the biologically active molecules are selected from the group consisting of carbohydrates, drugs, lipids, lipopolysaccharides, peptides, proteins, glycoproteins, single-stranded oligonucleotides, double-stranded oligonucleotides, polynucleotides, analogs of immunogens, haptens, mimotopes, and aptamers.

Claim 76 (previously presented): The composition of claim 64, wherein the chemically defined valency platform molecule is substantially nonimmunogenic.

Claim 77 (previously presented): The composition of claim 64 or 74, wherein the composition comprises a pharmaceutically acceptable carrier.

Claim 78 (cancelled)

Claim 79 (currently amended): The composition of claim 77, wherein the composition is suitable for injection in an individual.

Claim 80 (previously presented): The composition of claims 22, 64 or 74, wherein the valency platform molecule comprises polyethylene glycol having a molecular weight of about 200 to about 8,000.

Claim 81 (previously presented): The composition of claims 22, 64 or 74, wherein the conjugate comprises a moiety having the formula $-\text{CH}_2(\text{CH}_2\text{OCH}_2)_r\text{CH}_2-$, wherein $r = 1$ to 300.

Claim 82 (previously presented): The composition of claims 22, 64 or 74, wherein the valency platform molecule comprises a moiety having the formula $-\text{CH}_2(\text{CH}_2\text{OCH}_2)_r\text{CH}_2-$, wherein $r = 1$ to 300.

Claim 83 (cancelled)

Claim 84 (previously presented): The composition of claim 64 or 74, wherein the valency platform molecule comprises triethylene glycol.

Claim 85 (cancelled)

Claim 86 (previously presented): The composition of claim 64, wherein the valency platform molecules have substantially homogeneous molecular weight.

Claim 87 (cancelled)

Claim 88 (cancelled)

Claim 89 (previously presented): The composition of claim 64 or 74, wherein the conjugate comprises linking groups that bind the valency platform molecule to the biologically active molecules.

Claims 90-98 (cancelled)

Claim 99 (previously presented): The conjugate according to claim 89, wherein the linking group is derived from a thio-6 carbon chain phosphate or a thio-6 carbon chain phosphorothioate.

Claim 100 (previously presented): The conjugate of claim 89, wherein the linking group is derived from an alkylsulfhydryl moiety and the attachment sites comprise thiophilic groups.

Claim 101 (previously presented): The conjugate of claim 64 or 74, wherein the attachment sites are thiophilic groups.

Claim 102 (previously presented): The conjugate of claim 101, wherein the thiophilic groups are selected from the group consisting of haloacetyl, alkyl halide, alkyl sulfonate, maleimide, α,β -unsaturated carbonyl, alkyl mercurial, sulfhydryl, and α,β -unsaturated sulfone.

Claim 103 (previously presented): The conjugate of claim 101 wherein the attachment sites are selected from a maleimide, α -haloacetyl group or other appropriate Michael acceptor.

Claim 104 (previously presented): The conjugate of claim 103, wherein the attachment sites are α -haloacetyl groups.

Claim 105 (previously presented): The conjugate of claim 104, wherein the α -haloacetyl is bromoacetyl.

Claim 106 (currently amended): A conjugate formable by the conjugation of:

(a) a $-\text{OCH}_2\text{CH}_2\text{O}-$ $-\text{CH}_2\text{OCH}_2-$ containing chemically defined valency platform molecule, wherein:

- the valency platform molecule comprises branching groups that are derived from a diamino acid, triamine or amino diacid;
- the valency of said platform molecule is provided by at least four but no more than 32 or more attachment sites located at termini of the valency platform molecule; and
- the valency platform molecule is chemically defined in that the number of branching groups pre-determines the number of attachment sites; and

(b) a multiplicity of biologically active molecules wherein the biologically active molecules are polynucleotides.

Claim 107 (previously presented): The conjugate of claim 106, wherein the polynucleotides comprise a polynucleotide duplex.

Claim 108 (previously presented): The conjugate of claim 106 or 107, wherein each of the polynucleotides comprises at least 20 nucleotides.

Claim 109 (previously presented): The conjugate of claim 106, wherein each of said polynucleotides comprises a single stranded polynucleotide consisting of approximately 20 alternating cytosine (C) and adenosine (A) nucleotides.

Claim 110 (previously presented): The conjugate of claim 109, wherein a second single stranded polynucleotide consisting of approximately 20 alternating thymidine (T) and guanosine (G) nucleotides is annealed to each of said single stranded polynucleotides that consists of

approximately 20 alternating cytosine (C) and adenosine (A) nucleotides to form a double-stranded polynucleotide conjugate.

Claim 111 (currently amended): The conjugate of claim 26, 68, ~~[[64,]]~~ or 107, wherein said polynucleotides individually comprise the polynucleotide duplex of the formula:



Claim 112 (cancelled)

Claim 113 (previously presented): The conjugate of claim 106 or 110, wherein said polynucleotides are individually bound to the valency platform molecule via the 5' end of the polynucleotides.

Claim 114 (currently amended): The conjugate of claim 106 or 110, ~~110 or 111~~, wherein the polynucleotides are individually bound to the valency platform molecule via linker molecules.

Claim 115 (previously presented): The conjugate of claim 114 wherein each of the linker molecules is derived from a thio-6 carbon chain phosphate or a thio-6 carbon chain phosphorothioate.

Claim 116 (previously presented): The conjugate of claim 114, wherein the linker molecules are derived from an alkylamino or alkylsulfhydryl moiety.

Claim 117 (previously presented): The conjugate of claim 116, wherein the linker molecules are derived from an alkylsulfhydryl moiety.

Claim 118 (previously presented): The conjugate of claim 116, wherein the alkylamino or alkylsulfhydryl moiety is bound to the polynucleotide by phosphoramidite chemistry.

Claim 119 (currently amended): The conjugate of claim 106 or 110, ~~110 or 111~~, wherein the attachment sites are thiophilic groups.

Claim 120 (previously presented): The conjugate of claim 119, wherein the thiophilic groups are selected from the group consisting of haloacetyl, alkyl halide, alkyl sulfonate, maleimide, α,β -unsaturated carbonyl, alkyl mercurial, sulfhydryl, and α,β -unsaturated sulfone.

Claim 121 (previously presented): The conjugate of claim 119 wherein the attachment sites are selected from a maleimide, α -haloacetyl group or other appropriate Michael acceptor.

Claim 122 (previously presented): The conjugate of claim 119, wherein the attachment sites are α -haloacetyl groups.

Claim 123 (previously presented): The conjugate of claim 119, wherein the α -haloacetyl is bromoacetyl.

Claim 124 (currently amended): A composition comprising the conjugate of claim 106 or 110, ~~110 or 111~~ in a pharmaceutically acceptable carrier.

Claim 125 (currently amended): The conjugate of claim 106 or 110, ~~110 or 111~~, formulated with a pharmaceutically acceptable injectable vehicle.

Claim 126 (cancelled)

Claim 127 (cancelled)

Claim 128 (previously presented): A method of making the conjugate of claim 107, the method comprising:

reacting (a) a multiplicity of single-stranded polynucleotides, each of which is at least 20 nucleotides in length and has a functional group at or proximate one of its termini which is optionally derivatized with a linker group, with (b) attachment sites on the chemically-defined valency platform molecule to form the conjugate; and

annealing complementary single-stranded polynucleotides to the single-stranded polynucleotide conjugated to the chemically-defined valency platform molecule to form pendant chains of double-stranded polynucleotides.

Claim 129 (withdrawn): A method of making the composition of claim 64 or 106, the method comprising forming said conjugates by covalently bonding the biologically active molecules to the chemically-defined valency platform molecule to form a conjugate.

Claim 130 (previously presented): The composition of claim 64 or 74, wherein the valency platform molecule comprises 2,2'-ethylenedioxydiethylamine.

Claim 131 (previously presented): The composition of claim 64 or 74, wherein the valency platform molecule comprises $-\text{CH}_2(\text{CH}_2\text{OCH}_2)_r\text{CH}_2-$.

Claim 132 (previously presented): The composition of claim 80, wherein the conjugate comprises linking groups that bind the valency platform molecule to the biologically active molecules.

Claim 133 (previously presented): The composition of claim 84 wherein the conjugate comprises linking groups that bind the valency platform molecule to the biologically active molecules.

Claim 134 (previously presented): The conjugate of claim 106 or 107, wherein each of the polynucleotides comprises about 20 nucleotides.

Claim 135 (previously presented): A method of making the composition of claim 22, 64 or 106, wherein the biologically active molecules comprise a polynucleotide duplex, the method comprising forming said conjugates by:

reacting a multiplicity of single-stranded polynucleotides, each of which is about 20 nucleotides in length and has a functional group at or proximate one of its termini, with functional groups on the chemically-defined valency platform molecule to form the conjugate; and

annealing complementary single-stranded polynucleotides to the single-stranded polynucleotides conjugated to the chemically-defined valency platform molecule to form pendant chains of double-stranded polynucleotides.

Claim 136 (previously presented): A method of making the conjugate of claims 26, 68 or 107, the method comprising:

reacting (a) a multiplicity of single-stranded polynucleotides, each of which is about 20 nucleotides in length and has a functional group at or proximate one of its termini which is derivatized with a linker group, with (b) attachment sites on the chemically-defined valency platform molecule to form the conjugate; and

annealing complementary single-stranded polynucleotides to the single-stranded polynucleotide conjugated to the chemically-defined valency platform molecule to form pendant chains of double-stranded polynucleotides.

Claim 137 (previously presented): The composition of claim 26, 68 or 106, wherein the polynucleotide is a single stranded polynucleotide.

Claim 138 (previously presented): The composition of claim 69, wherein the branching groups are derived from a functional moiety selected from the group consisting of diamino acid, triamine, and amino diacid.

Claim 139 (previously presented): The composition of claim 69, wherein the composition comprises a pharmaceutically acceptable carrier.

Claim 140 (previously presented): A method of making the composition of claim 89, wherein the method comprises bonding the linker molecules to the polynucleotides and bonding the linker-polynucleotide to the valency platform molecule at the attachment sites to form the conjugate.

Claim 141 (previously presented): A method of making the composition of claim 89, wherein the method comprises bonding the linker molecules to the valency platform molecule at the attachment sites and bonding the linker-valency platform molecule to the polynucleotides to form the conjugate.

Claim 142 (previously presented): A method of making the composition of claim 129, the method comprising forming said conjugates by covalently bonding the polynucleotides to the chemically-defined valency platform molecule via a linker.

Claim 143 (currently amended): The composition of claim 64, wherein the biologically active molecules are selected from the group consisting of single-stranded oligonucleotides, double-stranded oligonucleotides, analogs of an immunogen, haptens, mimotopes, aptamers, polynucleotides, carbohydrates, lipids, lipopolysaccharides, peptides, proteins, glycoproteins, and drugs.

Claim 144 (previously presented): The composition of claim 77, wherein the composition is suitable for the suppression of antibody production.

Claim 145 (cancelled)

Claim 146 (currently amended): The composition of claim 77, wherein the composition is suitable for reducing antibody levels in an individual.

Claim 147 (previously presented): The composition of claim 77 wherein at least one molecule of the biologically active molecules is an analog of an immunogen that binds specifically to an antibody to which the immunogen binds specifically and lacks T cell epitopes.

Claim 148 (previously presented): The composition of claim 66, wherein the biologically active molecules comprise a polynucleotide.

Claim 149 (previously presented): A method of making the composition of claim 114, wherein the method comprises bonding the linker molecule to the biologically active molecule and bonding the linker-biologically active molecule to the valency platform molecule at the attachment sites to form the conjugate.

Claim 150 (previously presented): A method of making the composition of claim 114, wherein the method comprises bonding the linker molecule to the valency platform molecule at the attachment sites and bonding the linker-valency platform molecule to the biologically active molecules to form the conjugate.

Claim 151 (previously presented): The composition of claim 26, 68 or 106, wherein the polynucleotides comprise polynucleotide duplexes having significant binding activity for human systemic lupus erythematosus anti-dsDNA autoantibodies.

Claim 152 (previously presented): The composition of claim 151, wherein the polynucleotides comprise at least 20 base pairs.

Claim 153 (previously presented): The composition of claim 151, wherein the polynucleotides comprise about 20 base pairs.

Claim 154 (previously presented): The composition of claim 151, wherein the composition comprises a pharmaceutically acceptable carrier.

Claim 155 (currently amended): The composition of claim 26, 38, 68, 69, 70 or 107, ~~107 or 127~~, wherein the composition comprises a pharmaceutically acceptable carrier.

Claim 156 (previously presented): A method of making the composition of claim 64 or 106, wherein the biologically active molecules are a polynucleotide duplex, the method comprising forming said conjugates by:

reacting a multiplicity of single-stranded polynucleotides, each of which is at least 20 nucleotides in length and has a functional group at or proximate one of its termini, with functional groups on the chemically-defined valency platform molecule to form the conjugate; and

annealing complementary single-stranded polynucleotides to the single-stranded polynucleotides conjugated to the chemically-defined valency platform molecule to form pendant chains of double-stranded polynucleotides.

Claim 157 (new): The composition of claims 22, 64 or 106 wherein the conjugate has two branching groups, providing a total of four attachment sites for the biologically active molecules.

Claim 158 (new): The composition of claim 157 wherein each of the four biologically active molecules is the same.

Claim 159 (new): The composition of claims 22 or 64 wherein the biologically active molecule is a double-stranded polynucleotide.

Claim 160 (new): The composition of claims 22 or 64 wherein the biologically active molecule is a single-stranded polynucleotide.

Claim 161 (new): The composition of claim 159 wherein the polynucleotide is DNA.

Claim 162 (new): The composition of claim 160 wherein the polynucleotide is DNA.

Claim 163 (new): The composition of claim 161 wherein the polynucleotide has significant binding activity for human systemic lupus erythematosus anti-double stranded DNA autoantibodies.

Claim 164 (new): The composition of claim 162 wherein the polynucleotide is a single stranded polynucleotide of about 20 alternating cytosine (C) and adenosine (A) nucleotides.

Claim 165 (new): The composition of claim 162 wherein the single stranded polynucleotide is (CA)₁₀.

Claim 166 (new): The composition of claim 161 wherein the polynucleotide is a 20 base pair polynucleotide.

Claim 167 (new): The conjugate according to claim 161 wherein the DNA is 20 to 50 base pairs in length.

Claim 168 (new): The composition of claim 161 wherein the double stranded polynucleotide is a duplex of about 20 alternating cytosine (C) and adenosine (A) nucleotides annealed to about 20 alternating thymidine (T) and guanosine (G) nucleotides.